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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/624,909	07/21/2003	Eileen Tozer	D1410-2US	7087

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ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
03/21/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/624,909	TOZER ET AL.	
	Examiner	Art Unit	
	ANGELA BERTAGNA	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☒ Claim(s) *189* is/are allowed.

6)☒ Claim(s) *1,14,15,35,43-45,48,49,87,188,207,217,218,220 and 225-228* is/are rejected.

7)☒ Claim(s) *188 and 225-227* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1,14,15,35,42-45,48,49,87,111,113,116,138,143,174,175,177,182,184,187-190,207,208,217-229 and 231.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 42,111,113,116,138,143,174,175,177,182,184,187,190,208,219,221-224,229 and 231.

DETAILED ACTION

Status of the Application

1. Applicant's response filed on December 22, 2010 is acknowledged. Claims 1, 14, 15, 35, 42-45, 48, 49, 87, 111, 113, 116, 138, 143, 174, 175, 177, 182, 184, 187-190, 207, 218, 217-229, and 231 are currently pending. In the response, Applicant amended claim 1. Claims 42, 111, 113, 116, 138, 143, 174, 175, 177, 182, 184, 187, 190, 208, 219, 221-224, 229, and 231 remain withdrawn from consideration as being drawn to a non-elected invention.

The following include new grounds of rejection necessitated in part by Applicant's amendments to the claims. Any previously made objections or rejections not reiterated below have been withdrawn. Applicant's arguments filed on December 22, 2010 have been fully considered and are discussed in the "Response to Arguments" section. Since the new grounds of rejection set forth below were not entirely necessitated by Applicant's amendment, this office action is **NON-FINAL**.

Drawings

2. Applicant's submission of color drawings on July 21, 2003 is acknowledged. The submission of the fee set forth in 37 CFR 1.84(b)(2) on December 22, 2010 is also acknowledged. Since Applicant has complied with all of the requirements for submitting color drawings, the petition filed under 37 CFR 1.84(a)(2) has been granted.

/Gary Benzion/
Supervisory Patent Examiner, Art Unit 1637

Claim Objections

3. Claim 188 is objected to because of the following informalities: This claim contains markings to identify changes made in the last submission. As noted in 37 CFR 1.121 only the most recent changes should be identified with markings.

Claims 225-227 are objected to because of the following informalities: The recitation "and encoding a fluorescent protein" appears to be redundant in view of the amendments to claim 1, from which these claims depend.

Claim Rejections - 35 USC § 112, 1st paragraph (Written Description)

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 188 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a written description rejection.

The central inquiry when considering written description is whether an ordinary artisan would reasonably conclude that Applicant was in possession of the claimed invention at the time of filing (see MPEP 2163 and Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 1566-67, 43 USPQ2d 1398, 1404-05 (Fed. Cir. 1997); Hyatt v. Boone, 146 F.3d 1348, 1354, 47 USPQ2d 1128, 1132 (Fed. Cir. 1998)).

According to Revision I of the Written Description Training Materials (posted 4/11/08 at http://www.uspto.gov/web/menu/written/pdf), the following factors should be considered, when evaluating a claim for compliance with the written description requirement: (a) actual reduction to practice, (b) disclosure of drawings or structural chemical formulas (c) sufficient relevant identifying characteristics (d) method of making the claimed invention, (e) level of skill and knowledge in the art, and (f) predictability in the art (see page 1 of the Training Materials).

Claim 188 is drawn to isolated nucleic acids that encode a fluorescent polypeptide and are at least 97% identical to SEQ ID NO: 29. The genus of nucleic acids having at least 97% identity to SEQ ID NO: 29 is very large and includes hundreds of thousands of structurally distinct molecules, each of which may encode a polypeptide having different functional properties. The claims limit this large genus to nucleic acids that encode a fluorescent protein.

The specification teaches the nucleic acid sequence of SEQ ID NO: 29 (see page 17 of the Sequence Listing and page 37), and therefore, it contains an actual reduction to practice of one member within the claimed genus. The specification also discloses a nucleic acid that is at least 97% identical to SEQ ID NO: 29 and encodes a fluorescent protein (see Table 2 on page 124, where SEQ ID NO: 17, which is 99% identical to SEQ ID NO: 29 is taught). However, none of the other fluorescent proteins described in Table 2 on pages 124-125 of the specification fall within the claimed genus of nucleic acids. Also, neither the specification nor the prior art describes the regions of SEQ ID NO: 29 and those sequences at least 97% identical thereto that are critical for conferring fluorescence activity to the encoded protein, for example, by mutagenesis analysis, sequence analysis, or other methods. The claimed nucleic acids also do not share a high degree of similarity to other known fluorescent proteins, and, as a result, it is not

clear that the information available in the art concerning function-critical regions of other fluorescent proteins, such as GFP, would be applicable to the proteins encoded by the claimed nucleic acids. Furthermore, as evidenced by the specification of the instant application at page 129, for example, there is a high degree of unpredictability in the art regarding structure-function correlations, and even a single nucleotide substitution can abolish the function of the protein encoded by a mutant nucleic acid. Accordingly, the level of skill required in this unpredictable art is high. As a result, the specification clearly fails to adequately describe the relevant identifying characteristics that are critical for determining whether a particular nucleic acid with the claimed genera of nucleic acids having at least 97% identity to SEQ ID NO: 29 also possesses the required functional property of encoding a fluorescent protein. In the absence of such disclosure, it must be concluded that Applicant was not in possession of the claimed invention at the time of filing. Accordingly, claim 188 has been rejected under 35 U.S.C. 112, first paragraph for failing to comply with the written description requirement.

Claim Rejections - 35 USC § 112, 1st paragraph (Scope of Enablement)

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 188 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid that encodes a fluorescent protein and comprises SEQ ID NO: 29 or SEQ ID NO: 17, does not reasonably provide enablement for any other nucleic acids that are at least 97% identical to SEQ ID NO: 29 and that encode a

fluorescent protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claim.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Nature of the Invention & Breadth of the Claims

Claim 188 is drawn to isolated nucleic acids that encode a fluorescent polypeptide and are at least 97% identical to SEQ ID NO: 29. The genus of nucleic acids having at least 97% identity to SEQ ID NO: 29 is very large and includes hundreds of thousands of structurally distinct molecules, each of which may encode a polypeptide having different functional properties. The claim further limits this large genus to nucleic acids that encode a fluorescent protein.

Guidance in the Specification and Working Examples

The specification teaches the nucleic acid sequence of SEQ ID NO: 29 (see page 17 of the Sequence Listing and page 37), and, therefore, it contains an actual reduction to practice of one member within the claimed genus. The specification also discloses a nucleic acid that is at

least 97% identical to SEQ ID NO: 29 and encodes a fluorescent protein (see Table 2 on page 124, where SEQ ID NO: 17, which is 99% identical to SEQ ID NO: 29 is taught). However, none of the other fluorescent proteins described in Table 2 on pages 124-125 of the specification fall within the claimed genus of nucleic acids. Also, neither the specification nor the prior art describes the regions of SEQ ID NO: 29 and those sequences at least 97% identical thereto that are critical for conferring fluorescence activity to the encoded protein, for example, by mutagenesis analysis, sequence analysis, or other methods.

The working examples (see pages 155-159) also do not describe the regions of the disclosed nucleic acids that are critical for encoding a functional (i.e., fluorescent) protein. In Example 1 cDNA libraries prepared from marine sources were analyzed to identify cDNA clones encoding fluorescent proteins (see pages 155-156). In Example 2 (see pages 156-158), fluorescent proteins were isolated and purified. In Example 3 (see pages 158-159), the excitation and emission properties for a subset of the disclosed fluroescent proteins was determined. However, Examples 1-3 do not provide any discussion of regions of the proteins that are required for fluorescence activity.

State of the Prior Art and Unpredictability

The prior art does not teach isolated nucleic acids that are at least 97% identical to SEQ ID NO: 29 and encode a fluorescent polypeptide, and, therefore, the prior art does not identify the regions of the claimed nucleic acids that are critical for fluorescence activity. The claimed nucleic acids also do not show a significant level of similarity to other fluorescent proteins known in the art, and, as a result, it is not clear that the information available in the art

concerning function-critical regions of other fluorescent proteins, such as GFP, would be applicable to the proteins encoded by the claimed nucleic acids. Furthermore, there is a high degree of unpredictability in the art regarding structure-function correlations, and it is well established that even a single nucleotide substitution can abolish the function of the protein encoded by the mutant nucleic acid (see page 129 of the specification, for example). Therefore, it is highly unpredictable as to whether a nucleic acid having at least 97% identity to SEQ ID NO: 29 will possess fluorescence activity, particularly since neither the specification nor the art teaches the regions of the protein that are critical for this activity.

Quantity of Experimentation

The quantity of experimentation required in this case is immense, because it would require significant study and experimentation to determine whether a nucleic acid having at least 97% identity to SEQ ID NO: 29 also encodes a fluorescent protein. Each different variant nucleic acid would have to be produced via mutagenesis, and the encoded proteins would have to be expressed and characterized functionally. In the absence of any guidance in the specification or the art regarding regions of SEQ ID NO: 29 that are critical for determining fluorescence activity, the ordinary artisan would have little or no starting point for determining whether a given variant of SEQ ID NO: 29 encodes a fluorescent protein. Given the unpredictability in the art regarding the effect of nucleic acid mutations on the functionality of the proteins encoded therefrom, the ordinary artisan would be required to undertake this large quantity of experimentation with little or no guarantee of success.

The Level of skill in the art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, claim 188 is broadly drawn to isolated nucleic acids having at least 97% identity to SEQ ID NO: 29 and encoding a fluorescent protein. Despite the breadth of the claims, the specification only teaches a small number of nucleic acids falling within the claimed genus and provides no guidance regarding the regions of SEQ ID NO: 29 that are required for the fluorescence activity of the claimed proteins. Thus, given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to determine those regions of SEQ ID NO: 29 required for fluorescence activity, the lack of guidance provided in the specification, balanced only against the high skill level in the art, it is the position of the examiner that the claimed nucleic acid products fail to comply with the enablement requirement.

Claim Rejections - 35 USC § 112, 2nd paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 14, 15, 35, 43-45, 48, 49, 87, 207, 217, 218, 220, and 225-228 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 14, 15, 35, 43-45, 48, 49, 87, 207, 217, 218, 220, 225-228 are indefinite, because the scope of independent claim 1 is unclear. In particular, it is not clear how a nucleic acid sequence completely complementary to a nucleic acid sequence having at least 95% identity to SEQ ID NO: 29 can be considered to encode a fluorescent protein as set forth in SEQ ID NO: 30, since a nucleic acid that is completely complementary to a nucleic acid sequence having at least 95% identity to SEQ ID NO: 29 will necessarily encode a different protein. Amending the claim to replace "completely complementary to (a)" with "completely complementary to a nucleic acid sequence having at least 95% sequence identity to the nucleic acid sequence of SEQ ID NO: 29" would likely obviate this rejection.

Claims 14 and 15 are further indefinite, because it is unclear how the single fluorescent protein recited in claim 1, from which claims 14 and 15 depend, can comprise a green fluorescent protein and a cyan fluorescent protein as recited in these claims. It would appear that the protein of SEQ ID NO: 30 comprises either a green fluorescent protein or a cyan fluorescent protein unless the claims omit essential elements.

Allowable Subject Matter

7. Claim 189 is allowed.

Response to Arguments

8. Applicant's arguments filed on December 22, 2010 have been fully considered.

Objection to the Drawings

The response does not explicitly address the previously made objection. The objection has been withdrawn in view of the specification amendments, which have obviated the objection.

Objection to claim 188

Applicant argues that the amendment has obviated the previously made objection (page 16). This argument was persuasive, but the amendment has prompted a new objection to claim 188.

Rejection under 35 U.S.C. 112, first paragraph (written description)

In view of the claim amendments, the rejection currently applies to claim 188.

Applicant argues that the rejection has been obviated by the amendment to claim 1, which requires the nucleic acid to encode the fluorescent protein set forth in SEQ ID NO: 30 (page 17). This argument was persuasive with respect to all of the previously rejected claims except for claim 188, which does not depend from claim 1 and has not been amended in the response. As discussed above, the genus of nucleic acids encompassed by claim 188 is not adequately described, and, accordingly, the rejection has been maintained with respect to claim 188.

Rejection under 35 U.S.C. 112, first paragraph (scope of enablement)

In view of the claim amendments, the rejection currently applies to claim 188.

Applicant argues that the rejection has been obviated by the amendment to claim 1, which requires the nucleic acid to encode the fluorescent protein set forth in SEQ ID NO: 30 (page 17). This argument was persuasive with respect to all of the previously rejected claims except for claim 188, which does not depend from claim 1 and has not been amended in the

response. As discussed above, the genus of nucleic acids encompassed by claim 188 is not fully enabled by the disclosure, and, accordingly, the rejection has been maintained with respect to claim 188.

Conclusion

9. Claims 1, 14, 15, 35, 43-45, 48, 49, 87, 188, 217, 218, 220, and 225-228 are free of the art, but they have been rejected for failing to comply with the requirements of 35 U.S.C. 112. Claim 189 is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANGELA BERTAGNA whose telephone number is (571)272-8291. The examiner can normally be reached on M-F, 9- 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Angela M Bertagna/
Examiner, Art Unit 1637